UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/579,921	05/19/2006	Morgane Bomsel	BJS-3665-180	4876

23117 7590 06/11/2009
NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
NIEBAUER, RONALD T	
ART UNIT	PAPER NUMBER
1654	
MAIL DATE	DELIVERY MODE
06/11/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/579,921	BOMSEL ET AL.	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-44* is/are pending in the application.

4a) Of the above claim(s) *23-33 and 42-44* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/19/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election of Group I (claims 34-41) and the species of SEQ ID NO:9 (i.e. CysSerPheGluGluCys wherein a disulfide bond connects the Cys residues) in the replies filed on 9/8/08 and 2/2/09 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

It is noted that claim 38 and dependent claims are drawn to 'multimers'. It is noted that applicant has elected SEQ ID NO:9 (i.e. CysSerPheGluGluCys wherein a disulfide bond connects the Cys residues). As currently interpreted (see discussion with the art rejections below), the claims drawn to the multimers have been interpreted as reading on the elected species.

In the instant case, the prior art obviate the elected species. Any art that was uncovered during the search for the elected species that reads on non-elected species is also cited herein. In accord with section 803.02 of the MPEP the claims have been examined fully with respect to the elected species.

Claims 1-22 have been cancelled.

Claims 23-33,42-44 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 9/8/08 and 2/2/09.

Claims 34-41 are under consideration.

Claim Objections

Claims 36,40 are objected to because of the following informalities:

37 CFR 1.821(d) states:

"Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing " in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims, even if the sequence is also embedded in the text of the description or claims of the patent application."

In the instant case, claim 36 makes reference to a sequence comprising at least 4 specifically defined amino acids for which a general sequence (SEQ ID NO:16) has been provided. In accord with 37 CFR 1.821(d), a sequence identifier (i.e. SEQ ID NO:16) should be included with claim 36.

Claims 36 recites 'wherein said peptide having'. The grammar used is awkward. It would appear that the appropriate language would be 'wherein said peptide has'.

Claims 36,40 recite 'selected in the group'. The grammar used is awkward. It would appear that the appropriate language would be 'selected from the group'.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34-35,38-39,41 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 34 and dependent claims 35,41 refer to variants and derivatives. There is no standard art-recognized definition of variants or derivatives. The required structural features of a variant or derivative are unclear. For example, it is unclear if a single hydrogen atom would be a variant since all other elements could be varied such that they are deleted. The specification (page 7 for example) refers to variants and derivatives. However, a specific definition has not been provided. There is more than one reasonable interpretation of what falls within the scope of the claims.

Claim 34,38 and dependent claims 35,39,41 state 'm and n are comprised between 0 and 14'. The language used is confusing. Although the phrase 'comprising' (see MPEP section 2111.03) is recognized the phrase 'comprised between' is unclear. In the instant case, it is unclear if m and n can be zero. Further, it is unclear if the intent of claims 34,38 is such that the numbers are in reference to a combination of m and n or if the numbers refer to each of m and n. For example, it is unclear if m and n can each be 14. Further, the claims refer to an X variable. It is unclear if when m or n is greater than 1, if the X is always the same amino acid or if each occurrence of X can be different. For example if m is 2 it is unclear if Pro-Ala is within the scope of Xm since each X is different.

Claim 41 states 'a multimer as defined above'. However, no definition of multimer appears anywhere, let alone 'above'.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34-35,41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.
>
> Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:
>
> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279,

284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the

claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

Further, to provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include: a) the scope of the invention; b) actual reduction to practice; c) disclosure of drawings or structural chemical formulas; d) relevant identifying characteristics including complete structure, partial structure, physical and/or chemical properties, and structure/function correlation; e) method of making the claimed compounds; f) level of skill and knowledge in the art; and g) predictability in the art.

In the instant case, the claims are drawn to cyclic peptides or variants or derivatives. Although unclear (see 112 2nd) for purposes of examination the claims have been given the broadest reasonable interpretation (see MPEP section 2111). The term 'variant' has been interpreted such that any number of variations (i.e. deletions, substitutions, insertions, etc) can occur. The term 'derivative' has been interpreted such that any common structural feature (for example a hydrogen) would render a compound a derivative. Claims 34,38 and dependent claims have been interpreted such that m and n are independently 0-14, each occurrence of X can represent a different amino acid. Since no definition of multimer appears the term has been given the broadest reasonable interpretation.

(1) Level of skill and knowledge in the art/predictability in the art:

The level of skill in the art is high. There is unpredictability in predicting functional effects of replacements. It is not within the skill of the art to predict any and all replacements that

would result in variants and derivatives that increase the fusiogenic capacity of a gamete (see title of invention).

(2) Scope of the invention/Partial structure/disclosure of drawings:

In the instant case, the claims are drawn to cyclic peptides or variants or derivatives. Although unclear (see 112 2nd) for purposes of examination the claims have been given the broadest reasonable interpretation (see MPEP section 2111). The term 'variant' has been interpreted such that any number of variations (i.e. deletions, substitutions, insertions, etc) can occur. The term 'derivative' has been interpreted such that any common structural feature (for example a hydrogen) would render a compound a derivative. Claims 34,38 and dependent claims have been interpreted such that m and n are independently 0-14, each occurrence of X can represent a different amino acid. Since no definition of multimer appears the term has been given the broadest reasonable interpretation.

In considering the size of the genus, if m+n is 9 wherein each occurrence of X is any of the 20 naturally occuring amino acids and the tripeptide FEE is replaced with a tripeptide wherein each amino acid is any of the 20 naturally occurring amino there are at least 20^{12} (i.e. 4096000000000000) different peptides. Further, there are many non-natural amino acids and other peptides that could be considered variants or derivatives. As such, the genus is large.

The specification, for example, page 12 (SEQ ID NO:9) provides a specific example of a cyclic peptide. However, the peptide represenst a small fraction of the possible variety of peptides in the genus. One of skill in the art would not recognize that applicant was in possession of the claimed genus.

There is substantial variability in the genus. Since there are a substantial variety of componds possible within the genus, the examples do not constitute a representative number of species and do not sufficiently describe the genus claimed (see Gostelli above).

(3) Physical and/or chemical properties and (4) Functional characteristics:

The title of the application states that the peptides increase the fusiogenic capacity of a gamete. The specification (page 7) states that the variants and/or derivatives increase the fusiogenic capacity and/or to activate oocytes. It is unclear what specific structural elements are required for the recited function. There is not an adequate correlation between structure and function. There are no common attributes or characteristics that identify all of the variants and derivatives. As such, one of skill in the art would not recognize a core structure, common attributes, or features of the variants and derivatives. One of skill in the art would not recognize variants and derivatives outside of those specifically identified. There is no teaching in the specification regarding what part of the structure can be varied while retaining the ability to increase the fusiogenic capacity and/or to activate oocytes. In particular, no common core sequence is taught for all of the variants and derivatives. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus and that there is a lack of the knowledge in the art regarding which amino acids can vary to maintain the function and thus that the applicant was not in possession of the claimed genus.

(5) Method of making the claimed invention/actual reduction to practice:

The specification (specifically page 12) describes the use of a cyclic peptide. However, such peptide is not representative of the instant genus nor does the peptide provide a specific

correlation between structure and function such that one could identify any and all variants and derivatives.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that claim(s) 34-35,41 is/are broad and generic, with respect to all possible compounds encompassed by the claims. The possible structural variations are many. Although the claims may recite some functional characteristics, the claims lack written description because there is no specific disclosure of a correlation between function and structure of the compounds beyond those compounds specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of compounds identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of compounds embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 34,41 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Myles et al (PNAS v91 pages 4195-4198 1994 as cited in IDS 5/19/06) teach sequences of peptides from guinea pig fertilin, for example (Figure 1) which include the sequence DEC. The recited peptide is a derivative (or variant) as recited in claim 34 where the cyclic part has been deleted and D has been changed to F and C has been changed to E. Since the peptide is present in guinea pig it is necessarily part of a composition as recited in claim 41

There is no indication that the peptides of the current invention have been isolated or removed from a naturally occurring environment. The claimed subject matter therefore reads on a product of nature.

Although unclear (see 112 2nd) for purposes of examination the claims have been given the broadest reasonable interpretation (see MPEP section 2111). The term 'variant' has been interpreted such that any number of variations (i.e. deletions, substitutions, insertions, etc) can occur. The term 'derivative' has been interpreted such that any common structural feature (for example a hydrogen) would render a compound a derivative. Claims 34,38 and dependent claims have been interpreted such that m and n are independently 0-14, each occurrence of X can represent a different amino acid. Since no definition of multimer appears the term has been given the broadest reasonable interpretation.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 34-35,38,41 are rejected under 35 U.S.C. 102(b) as being anticipated by Myles et al (PNAS v91 pages 4195-4198 1994 as cited in IDS 5/19/06).

Myles teach the binding site in fertilin required for sperm-egg fusion (title). Myles study the role of fertilin by using peptide analogues (abstract). Myles teach (page 4196 in particular Figure 1b) the cylcized peptide CSTDEC which was cyclized by oxidation (page 4196 2nd column 1st paragraph). Myles teach that the peptide was cyclized to better mimic the native binding site (page 4196 first column last paragraph). Myles teach that the peptides were conjugated to Covaspheres (page 4195 2nd column). The peptide of Myles includes the sequence TDE. In comparision to claims 34-35 the peptide of Myles is a variant (or derivative) wherein F is substituted with T, D is substituted with E, and wherein m+n is 3 thus meeting the limitations as recited in claims 34-35 of the instant invention. Since the peptide of Myles comprises the tripeptide TDE the TriPept limitations of claim 38 is met. It is noted that claim 38 recites 'multimer'. However, there is no structural requirement that the 'multimer' include direct linkages. For example, the art recognizes dimers which do no require direct linkages but which are held together by weak intermolecular forces. In the instant case, Myles expressly teach that

the peptides were conjugated to Covaspheres (page 4195 2nd column) so the peptides are multimers. Since Myles teach that the peptides were used in assays (see Table 2 results for example) the peptides were present in a composition as recite in claim 41. It is noted that claim 41 recites 'intended for gamete culture'. Such statement is an intended use which does not result in a structural difference. Thus, Myles meet the claim limitations.

Although unclear (see 112 2nd) for purposes of examination the claims have been given the broadest reasonable interpretation (see MPEP section 2111). The term 'variant' has been interpreted such that any number of variations (i.e. deletions, substitutions, insertions, etc) can occur. The term 'derivative' has been interpreted such that any common structural feature (for example a hydrogen) would render a compound a derivative. Claims 34,38 and dependent claims have been interpreted such that m and n are independently 0-14, each occurrence of X can represent a different amino acid. Since no definition of multimer appears the term has been given the broadest reasonable interpretation.

Claims 34-35,38-39,41 are rejected under 35 U.S.C. 102(b) as being anticipated by Krstenansky et al (Biochimica et biophysica acta 957 (1988) 53-59).

Krstenansky teach synthetic peptides cyclized via disulfide linkages (abstract). Krstenansky teach that peptide were synthesized and that monomers were separated from oligomers (connecting sentence of column 1 and 2 of page 54) and that evidence for cyclization was obtained (page 54 2nd column). Krstenansky specifically teach the cyclic peptide (cyclized via disulfide linkages) of sequence CDFEEIPEEYLC (compound 2 of Table I). Such peptide meets the limitations of claims 34-35 of the instant claims since m+n is 9 and the peptide

includes the tripeptide FEE. Since Krstenansky teach that peptides were synthesized and that monomers were separated from oligomers (connecting sentence of column 1 and 2 of page 54), multimers were necessarily present as recited in claims 38-39. Since Krstenansky teach that the peptides were used in assays (page 54 for example) the peptides were present in a composition as recited in claim 41. It is noted that claim 41 recites 'intended for gamete culture'. Such statement is an intended use which does not result in a structural difference. Thus, Krstenansky meet the claim limitations.

Although unclear (see 112 2nd) for purposes of examination the claims have been given the broadest reasonable interpretation (see MPEP section 2111). The term 'variant' has been interpreted such that any number of variations (i.e. deletions, substitutions, insertions, etc) can occur. The term 'derivative' has been interpreted such that any common structural feature (for example a hydrogen) would render a compound a derivative. Claims 34,38 and dependent claims have been interpreted such that m and n are independently 0-14, each occurrence of X can represent a different amino acid. Since no definition of multimer appears the term has been given the broadest reasonable interpretation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 34-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gupta et al (Bioorganic and Medicinal Chemistry v8(2000) pages 723-729 as cited in IDS 5/19/06) and Bronson et al (Molecular Human Production v5 (1999) pages 433-440 as cited in IDS 5/19/06) and Myles et al (PNAS v91 pages 4195-4198 1994 as cited in IDS 5/19/06).

Gupta teach that an essential step leading to fertilization is the binding of sperm to egg (abstract). Gupta teach that fertilinBeta is a protein on the surface of sperm that mediates the binding (abstract). Gupta teach that fertilinBeta contains a highly conserved motif (D/E)ECD which suggests it could be a consensus sequence (abstract). Gupta teach that a series of linear and cyclic peptides were synthesized to characterize the binding specificity (abstract, title).

Gupta does not expressly teach the elected species of the instant invention (i.e. SEQ ID NO:9 (i.e. CysSerPheGluGluCys wherein a disulfide bond connects the Cys residues)).

Gupta does show a sequence alignment for various species and teach that the binding loop for the human sequence is RPSFEECDLP (Figure 1). Gupta teach that several peptides

were synthesized (page 725, Figure 2) including cyclic peptides. Gupta recognize a goal of establishing the minimal number of amino acids in the putative binding loop of fertinlinBeta required for adhesion to the egg and the development of better peptidomimetic inhibitors (page 726 first column). Gupta recognize that peptides containing flanking residues (in relation to (D/E)ECD) have been tested (page 726 first column). Gupta teach that cyclic peptides were synthesized because cyclization should reduce the peptides entropy and increase binding affinity for its receptor (page 726 2nd column). Gupta teach that they can not yet conclude how many adjacent residues are required for binding (page 727 first column).

Since Gupta teach the development of better peptidomimetic inhibitors (page 726 first column) and teach that they can not yet conclude how many adjacent residues are required for binding (page 727 first column) one would be motivated to fine tune the experiments and determine specific peptides and peptide sequences for binding.

Bronson et al also teach that fertilin is a protein important for sperm-egg fusion (abstract). Bronson teach studies to evaluate fertlininBeta role in human fertilization by studying peptides containing an FEE sequence (abstract). Bronson teach that the FEE containing peptide inhibited adhesion of spermatozoa to eggs (page 435 2nd column). Bronson teach that the tripeptide FEE has been proposed to act as an integrin recognition site (page 438 2nd column).

Myles et al also teach the binding site in fertilin required for sperm-egg fusion (title). Myles study the role of fertilin by using peptide analogues (abstract). Myles teach (page 4196 in particular Figure 1b) the cylcized peptide CSTDEC based on guinea pig fertilin beta which was cyclized by oxidation (page 4196 2nd column 1st paragraph). Myles teach that the peptide was

cyclized to better mimic the native binding site (page 4196 first column last paragraph). Myles teach that the peptides were conjugated to Covaspheres for use in assays (page 4195 2nd column).

From the sequence alignment shown in Figure 1 of Gupta one can see that the CSTDEC guinea pig fertilin beta sequence (wherein the first C is introduced for cyclization) corresponds to the sequence CSFEEC of the human sequence (wherein the first C is introduced for cyclization). In other words the guinea pig sequence is STDEC and the corresponding human sequence is SFEEC.

Taken together, the references recognize the use of peptides to study the binding intereactions of fertilinBeta with eggs. Since Gupta teach the development of better peptidomimetic inhibitors (page 726 first column) and teach that they can not yet conclude how many adjacent residues are required for binding (page 727 first column) one would be motivated to fine tune the experiments and determine specific peptides and peptide sequences for binding. Bronson recognizes the utility of studying the human fertilinBeta and suggests that the FEE sequence is a key region. Myles recognizes the use of cyclic peptides and specifically particular regions of the guinea pig fertilinBeta.

In summary, all of the references are focused on a core sequence of fertilinBeta either from humans or guinea pig. The references, including Gupta recognize the development of better peptidomimetic inhibitors (page 726 first column) as a goal.

Gupta does show a sequence alignment (Fig 1) for various species and teach that the binding loop for the human sequence is: RPSFEECDLP
and the loop for the guinea pig sequence is: RESTDECDLP (Figure 1).
Bronson teach the importance of the human FEE (abstract).

Myles teach the guinea pig based sequence CSTDEC (figure 1b where the C residues are linked via a disulfide).

Taken together, based on the suggestions of the references one would be motivated to make peptides corresponding to particular regions of the human fertilinBeta protein. Since Myles teach that the peptide was cyclized to better mimic the native binding site (page 4196 first column last paragraph) one would be motivated to make cyclic peptides, particularly by incorporating cysteine residues at the N and C-terminus of a 6 amino acid sequence. Since Bronson teach the importance of the FEE sequence and the guinea pig peptide taught by Myles includes the corresponding residues of the guinea pig peptide one would be motivated to make the following peptide: CSFEEC where the Cys residues are linked via a disulfide bond. In other words, Myles teach the guinea pig based (i.e. from RESTDECDLP) CSTDEC peptide (wherein the Cys residues are linked via a disulfide). The corresponding human based (i.e. from RPSFEECDLP) peptide is CSFEEC where the Cys residues are linked via a disulfide bond. Since Bronson teach the use of human based peptides and specifically teach the importance of including the FEE sequence one would be motivated to use human based sequences. One would have a reasonable expectation of success based on the teachings of the references.

Since the references obviate the following peptide CSFEEC where the Cys residues are linked via a disulfide bond, the limitations of claims 34-37 are met since m+n is 3 and the other structural limitations are met. It is noted that claim 38 recites 'multimer'. However, there is no structural requirement that the 'multimer' include direct linkages. For example, the art recognizes dimers which do no require direct linkages but which are held together by weak intermolecular forces. Since Myles teach that the peptides were conjugated to Covaspheres for use in assays

(page 4195 2nd column) one would be motivated to conjugate the peptides (i.e. CSFEEC where the Cys residues are linked via a disulfide bond) to Covaspheres for ease of use in assays therefore meeting the multimer limitation as recited in claims 38-40. Since the peptides are taught to be tested in assays, one would be motivated to include the peptides in compositions as recited in claim 41. It is noted that claim 41 recites 'intended for gamete culture'. Such statement is an intended use which does not result in a structural difference. Thus, the references render obvious the claim limitations.

Although unclear (see 112 2nd) for purposes of examination the claims have been given the broadest reasonable interpretation (see MPEP section 2111). The term 'variant' has been interpreted such that any number of variations (i.e. deletions, substitutions, insertions, etc) can occur. The term 'derivative' has been interpreted such that any common structural feature (for example a hydrogen) would render a compound a derivative. Claims 34,38 and dependent claims have been interpreted such that m and n are independently 0-14, each occurrence of X can represent a different amino acid. Since no definition of multimer appears the term has been given the broadest reasonable interpretation.

Prior Art of Record

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Evans et al (Journal of Cell Science 108(1995) pages 3267-3278 as cited in IDS 5/19/06). Evans teach cyclic peptides of fertilin specifically from mouse (abstract). Evans teach the cyclic peptide CAQDEC. Gupta et al (cited above) teach (Figure 1) the mouse and human fertilinBeta binding loops:

Mouse: RLAQDECDVT

Human: RPSFEECDLP

Thus the mouse CAQDEC peptide corresponds to human CSFEEC. Any rejection using Evans would be duplicative of the rejections above.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ronald T Niebauer/
Examiner, Art Unit 1654

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 1654